PATENT
ATTORNEY DOCKET NO. 28967/35255A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Ferrell *et al.*

Serial No. 09/375,248

Filed: August 16, 1999

Title: SCREENING AND THERAPY FOR LYMPHATIC DISORDERS INVOLVING THE FLT4 RECEPTOR TYROSINE KINASE (VEGFR-3)

Group Art Unit: 1634

Examiner: Betty J. Forman

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on 5 February 2003

David A. Gass
Reg. No. 38,153
Attorney for Applicants

Commissioner for Patents
Washington, DC 20231

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. ROBERT FERRELL

Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Dr. Robert Ferrell, do hereby declare and state as follows:

1. I am familiar with the contents of the above-identified U.S. patent application (hereinafter, the "patent application") and with the official action from the United States Patent and Trademark Office (hereinafter, the "Patent Office") dated August 6, 2002, a copy of which is attached hereto as Exhibit A. A copy of the amended claims that I understand will be filed for the patent application with this declaration are attached hereto as Exhibit B. I make this declaration for the following purposes:

a. to provide facts known to me that may be relevant to the issue of inventorship in the present application; and

b. to provide facts relating to Ferrell *et al.*, "Hereditary lymphedema: evidence for linkage and genetic heterogeneity," *Human Molecular Genetics, 7(13)*: 2073-2078 (1998), which facts may be pertinent to the Patent Office's rejections

under 35 U.S.C. §102(a) of claims 1-4, 6-10 and 37-38, and under 35 U.S.C. §103(a) of claims 5 and 11.

2. I am a named co-inventor of the subject matter of one or more claims in the patent application, as well as a named co-author of the Ferrell *et al.* paper. I am familiar with the contributions made by all of the co-authors of the paper to the subject matter reported in the paper. By virtue of communications with Kari Alitalo and Marika Karkkainen as part of a research collaboration between our laboratory in the United States and their laboratory in Finland, I am also familiar with the contributions made by Kari Alitalo and Marika Karkkainen to the subject matter of the patent application.

3. The Ferrell *et al.* article describes, summarizes, and analyzes genetic linkage analysis involving families having members that exhibit familial (hereditary) lymphedema. These studies allowed the identification of markers on human chromosome 5 that are linked with the occurrence of hereditary lymphedema. As reported in the paper, we identified a missense mutation in the *Flt4* (VEGFR-3) gene coding sequence of members of one family as a plausible candidate predisposing family members to familial lymphedema. The work summarized in this paper was performed largely by the team of co-authors listed on the article. However, David Finegold and I are the individuals that conceived the project and how to perform it, and interpreted the data. The contributions of the other co-authors reflect work performed under the direction and control of David Finegold and I. The other coauthors of Ferrell *et al.* (*i.e.*, Kara Levinson, Judith Esman, Mark Kimak, Elizabeth Lawrence, and M. Michael Barmada), were not listed as co-inventors of the application because their contributions were made under the direction and supervision of David Finegold or me.

4. As noted in the paper, the data provided in the paper identified Flt4 as both a positional and biologically plausible candidate gene for hereditary lymphedema, but assessment of the potential role of Flt4 in lymphedema at that time awaited a detailed mutation analysis. (Ferrell *et al.*, page 2077, first column.) Our laboratory collaborated with Kari Alitalo and Marika Karkkainen in Finland, who conducted the functional analysis (e.g., Flt4 signaling studies) reported in the patent application but not reported in the paper. Through the work of Kari Alitalo and Marika Karkkainen, for example, the collaboration

discovered that a Flt4 mutation reported in the Ferrell *et al.* paper reduces ligand-mediated signaling relative to the wild type Flt4/VEGFR-3 polypeptide. Kari Alitalo and Marika Karkkainen made other contributions to the project and the patent application as well.

5. I further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (18 U.S.C. § 1001), and may jeopardize the validity of the application or any patent issuing thereon.

Date 01/27/03

Dr. Robert Ferrell